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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,872	10/22/2003	Jane Hirsh	CP 107P	6830

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EXAMINER	
SCHLIENTZ, LEAH H	
ART UNIT	PAPER NUMBER
1618	

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08/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/690,872	HIRSH ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 6/01/2007, in reply to the Office Action mailed 3/26/2007, is acknowledged and has been entered. Claims 23 and 24 have been cancelled. Claims 1 – 22 are pending, and are examined herein on the merits for patentability.

Inventorship

In view of the papers filed 7/16/2007, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by the addition of Srinivas G. Rao.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Response to Arguments

Applicant's arguments filed 6/01/2007 have been fully considered but they are not persuasive for reasons set forth hereinbelow.

Claim Rejections - 35 USC § 112

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons set forth in the Office Action mailed 3/26/2007.

Applicant argues on page 9 of the Response that claim 13 specifies that the milnacipran is in the form of a therapeutically equivalent dose of an active metabolite of milnacipran or pharmaceutically acceptable salts thereof. Applicant contends that the specification discloses that metabolism of milnacipran in the liver leads to the formation of ten chemically identified metabolites, citing Puozzo *et al.*, *Eur. J. Drug. Metab. Pharmacokinet.*, Apr-Jun, 23(2), 273-279 (1998), which describes a few of these 10 metabolites including glucuroconjugated phase 1 metabolites, N-mono-dealkylated metabolites, N-di-dealkylated metabolites and hydroxylated metabolites, and that one of ordinary skill in the art would understand the bounds of the term "metabolite" when read in light of the specification.

This is non-persuasive because the claims are drawn to a therapeutically equivalent dose of an active metabolite of milnacipran. It is unclear what amount of any metabolite is to represent a therapeutically effective amount which should be included in the formulation. For example, the Puozzo *et al.* reference, while identifying a few metabolites of milnacipran (including free or glucuroconjugated phase 1 inactive metabolites, N-mono-dealkylated metabolites, etc.), further teaches that the unchanged drug is the only compound responsible for the activity of milnacipran (page 279, last

sentence). Thus it is unclear how one is to formulate a therapeutically effective dose of such metabolites, as they appear to be inactive compared to milnacipran.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1 – 10, 15 – 17 and 19 – 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Midha in view of Ansseau for reasons set forth in the Office Action mailed 3/26/2007.

Applicant argues on pages 14 – 18 of the Response that the combined teachings of Midha in view of Ansseau do not disclose or suggest a pulsatile release milnacipran formulation which provides a therapeutic effect over 24 hours with reduced incidence of intensity of side effects. Applicant contends that Midha is concerned with the pulsatile delivery of methylphenidate due to its potential for tolerance, short half-life, and potential for abuse and that milnacipran does not exhibit potential for tolerance or abuse. Applicant further argues that Midha does not recognize that pulsatile release formulations can be used to minimize side effects. In addition, applicant argues that Midha teaches away from formulations that provide a therapeutic effect over 24 hours because in pulsatile release formulations containing three doses, the third does should be lower than the first two due to the fact that methylphenidate can disrupt sleep and thus compositions described in Midha are not designed or intended to provide a therapeutic effect over 24 hours. Regarding the Ansseau reference, applicant argues

that Ansseau teaches an immediate release dose which is unlikely to provide therapeutic effect over 24 hours. Applicant contends that one would not be motivated to combine the pulsatile release formulations of Midha with the immediate release milnacipran formulations of Ansseau to arrive at the claimed compositions since neither reference discloses or suggests pulsatile release formulations that provide a therapeutic effect over 24 hours with reduced frequency or severity of side effects.

This is non-persuasive because, as cited in the Office Action mailed 3/26/2007, Midha teaches that pulsatile release formulations, including those having a release profile within the claimed range, are useful for drugs which have a short half-life and must otherwise be administered two or three times daily (column 1, lines 18+). One would have been motivated to provide milnacipran in such a pulsatile release dosage form because Ansseau specifically teaches that milnacipran has only a 7 hour plasma elimination half-life, and has previously been administered in two divided daily doses (page 136). The limitations such as reduced incidence or severity of side effects are functional in nature and would be an inherent property of such a formulation. The instant claims are defined only by function and are devoid of any structural limitations which might be used to distinguish over the cited references. C_{max} values of a given drug are also inherent properties of a given formulation. In the absence of evidence to the contrary, it is interpreted that the combined teachings of the pulsatile release formulation of a drug having a short half life, which must otherwise be provided in two separate doses, such as milnacipran, would be capable of the claimed release profile because the pulsatile release formulations taught by Midha are achieved via the same

coatings, etc. Regarding Applicant's argument that milnacipran does not exhibit potential for abuse, this is not found persuasive because Midha only teaches that pulsatile release formulations are useful for drugs having short half-lives which must be administered two or three times daily, and that such formulations are also useful for minimizing the abuse potential of certain types of drugs, however, Midha does not exclusively teach that only drugs having both qualities (i.e. short half-life and potential for abuse) are necessary. Regarding applicant's contention that Midha teaches away from a formulation having a therapeutic effect over 24 hours, this is not found persuasive because Midha only teaches reduced dosage at night, and does not teach a complete lack of therapeutic effect at night.

Claims 1 – 10 and 15 – 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Midha in view of Ansseau, in further view of Menza for reasons set forth in the Office Action mailed 3/26/2007.

Applicant argues on pages 18 – 19 of the Response that the combined teachings of Midha in view of Ansseau do not disclose or suggest a pulsatile release milnacipran formulation which provides a therapeutic effect over 24 hours with reduced incidence of intensity of side effects, and that Menza does not provide the elements missing from Midha and Ansseau.

This is non-persuasive for reasons set forth above, and because Menza teaches that modafinil is an augmenter to antidepressants in the treatment of depression.

Claims 1 – 13, 15 – 17 and 19 – 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Midha in view of Ansseau, in further view of Paillard for reasons set forth in the Office Action mailed 3/26/2007.

Applicant argues on pages 20 – 21 of the Response that the combined teachings of Midha in view of Ansseau do not disclose or suggest a pulsatile release milnacipran formulation which provides a therapeutic effect over 24 hours with reduced incidence of intensity of side effects, and that Paillard does not provide the elements missing from Midha and Ansseau.

This is non-persuasive for reasons set forth above, and because Paillard teaches that cis and trans enantiomers may be used in modafinil formulations for the treatment of depression.

Claims 1 – 3, 6 – 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rao *et al.* (US 2003/0203055) for reasons set forth in the Office Action mailed 3/26/2007.

Applicant argues on page 22 of the Response that Rao does not disclose a pulsatile release formulation, citing that "Example 41 in Rao describes a formulation containing an immediate release and sustained release doses." Applicant further contends that "a pulsatile release formulation is characterized by a first does of drug followed by a period of no release, followed by release of a delayed release dose, etc."

This is non-persuasive because Rao teaches a multilayer tablet having an immediate release portion and a sustained release portion. In the absence of evidence

to the contrary, such a formulation would result in at least one "pulse" of the active ingredient upon dissolution of the immediate release layer of the tablet, and then at least some additional release of active agent upon dissolution of the delayed release portion of the multilayer coatings. The instant claims are defined only by function and are devoid of any structural limitations, other than that the composition comprises a coating, which is also present in the formulations taught by Rao *et al.*

Double Patenting

Claims 1 – 9 and 11 – 22 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1 – 4 and 10 – 26 of copending Application No. 11/192,697. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Applicant argues on page 24 of the Response that "Claims 1 – 22 in U.S.S.N. 10/690,872 will be cancelled" and accordingly the rejection under 35 U.S.C. 101 is no longer applicable.

This is non-persuasive because claims 1 – 22 have not been cancelled in either the instant application (10/690,872) or the 11/192,697 application at this time. Thus, the claims stand rejected.

Claims 1 – 3, 6 – 19 and 20 – 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 3, 6 – 18 and 20 – 22 of copending Application No. 10/691,936 in view of Midha in

further view of Ansseau. This is a provisional obviousness-type double patenting rejection.

Applicant argues on pages 24 – 25 of the Response that the claims of the instant application are drawn to a pulsatile release formulation of milnacipran to produce a therapeutic effect over approximately 24 hours when administered to a patient in need, with diminished incidence or reduced intensity relative to one or more immediate release milnacipran side effects, while the claims of the '936 application are directed to a delayed or extended release formulation of milnacipran. Applicant states that the citation of Midha and Ansseau to provide elements missing from the claims of the '936 application is improper.

This is non-persuasive because a double patenting rejection of the obviousness-type is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, any analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). The Midha and Ansseau references were included to show that extended release and pulsatile release formulations of a drug having a short half-life, such as milnacipran, are obvious variants of one another. The copending claims are defined only by function and are devoid of any structural limitations to distinguish over one another. Applicant has provided no arguments to demonstrate that pulsatile

and extended release formulations of milnacipran which produce a therapeutic effect over approximately 24 hours when administered to a patient in need, with diminished incidence or reduced intensity relative to one or more immediate release milnacipran side effects are not obvious variants of one anther. Accordingly, the claims stand rejected.

Claim 14 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 3 and 9 of U.S. Patent No. 7,038,085 in view of Midha in further view of Anseau.

Applicant argues on page 26 of the Response that the claims of the instant application are drawn to a pulsatile release formulation of milnacipran to produce a therapeutic effect over approximately 24 hours when administered to a patient in need, with diminished incidence or reduced intensity relative to one or more immediate release milnacipran side effects, while the claims of the '085 patent are directed to a an isolated compound of formula A and B, respectively. Applicant states that the citation of Midha and Ansseau to provide elements missing from the claims of the '085 patent is improper.

This is non-persuasive because a double patenting rejection of the obviousness-type is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, any analysis employed in an obviousness-type double patenting rejection

parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). The Midha and Ansseau references were included to show that pulsatile release formulations are obvious formulations of a drug, such as milnacipran, which have a short half-life. The claims are defined only by function and are devoid of any structural limitations to distinguish over the pharmaceutical formulation of the claimed compound (i.e. claim 9 of the '085 patent).

Conclusion

No claims are allowed at this time.

Although Applicant's arguments as set forth in the aforementioned Response have been fully considered, they are deemed unpersuasive. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

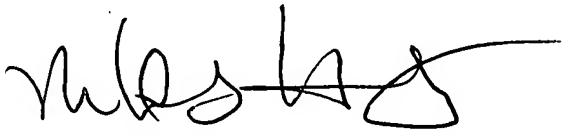
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LHS



MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER